Scientific Abstract

This investigation will estimate the maximum tolerated and dose-limiting toxicities of an adenoviral vector delivering the Herpes simplex transgene (AdV/RSV-TK) injected directly into retinoblastoma followed by the intravenous administration of ganciclovir every 12 hours for 7 days.

Retinoblastoma is the most common primary malignant tumor of children and usually occurs in children under the age of 3 years. Current standard treatment for nonmetastatic retinoblastoma is enucleation. Although this results in a high rate of survival, enucleation results in blindness and severe cosmetic facial deformity. Recently, attention has been turned to finding alternative therapies that will result in a high cure rate but will allow salvage of the affected eye. Occasionally a child presents with a small tumor that can be eradicated with cryotherapy or laser photocoagulation while still preserving the eye and useful vision. Unfortunately, most children present with tumors that are too large for these types of therapies. In an attempt to shrink a larger tumor to a size that can be managed by these local therapies, clinical investigators have begun trials using systemic chemotherapy instead of enucleation. Although preliminary studies have shown promise, chemotherapy has significant side effects including an increased rate of second malignancies. Because patients with retinoblastoma have a significant second malignancy potential, especially osteogenic sarcoma, as a natural course of their disease, an alternative therapy without systemic toxicity would be desirable.

Preclinical studies using AdV-mediated TK gene therapy have shown a high rate of success in shrinking retinoblastoma in an animal model of this disease. Based on these data, we propose to use this suicide gene therapy approach to shrink the retinoblastoma in children to a size that can be managed with local therapy.